CLAIMS

1. A compound including a heterocyclic nucleobase attached to a first carbon atom of an optionally substituted five-member saturated or monounsaturated heterocyclic group selected from tetrahydrofuranyl, tetrahydrothienyl, dihydrofuranyl and dihydrothienyl and further including a phosphonoalkoxy or phosphonothioalkyl group attached to a second carbon atom of said five-member saturated or mono-unsturated heterocyclic group, said first carbon atom being adjacent to the heteroatom of said five-member saturated or mono-unsturated heterocyclic group, and said second carbon atom being adjacent neither to the heteroatom nor to the first carbon atom of said five-member saturated or mono-unsturated heterocyclic group, said compound being represented by one of the general formulae (II) and (XIX):

(II), and

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$$R^{8}$$
 X^{1}
 B
 R^{3}
 R^{2}
 X^{4}
 X^{1}
 X^{2}
 X^{4}
 X^{1}
 X^{2}
 X^{4}
 X^{1}
 X^{2}
 X^{4}
 X^{1}
 X^{2}
 X^{3}
 X^{4}
 X^{4}

wherein:

- X¹, X², X³, X⁴ and X⁵ are each each independently selected from the group consisting of oxygen and sulfur,
- 20 B is a natural or non-natural heterocyclic nucleobase,

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R1 and R2 are each independently selected from the group consisting of (-PO₃R¹⁶)_m-PO₃R¹⁷R¹⁸; cvcloalkvl; alkyl; alkenvl; alkynyl; hydrogen; cycloalkenyl; cycloalkynyl; aryl; arylalkyl; heterocyclic; heterocyclic-alkyl; acyloxyalkyl; acyloxyalkenyl; acyloxyalkynyl; acyloxyarylalkyl; acyloxyarylalkenyl; acyloxyarylalkynyl; dialkylcarbonate; alkylarylcarbonate; alkylalkenylcarbonate; alkylalkynylcarbonate; alkenylarylcarbonate; alkynyldialkenylcarbonate; dialkynylalkenylalkynylcarbonate; arvicarbonate; carbonate; wherein said alkyl, alkenyl and alkynyl optionally contains one or more heteroatoms in or at the end of the hydrocarbon chain, said heteroatoms being independently selected from the group consisting of oxygen, sulfur and nitrogen;

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- R³, R⁴, R⁵, R⁶, R⁷ and R⁸ are each independently selected from the group consisting of hydrogen, azido, halogen, cyano, alkyl, alkenyl, alkynyl, SR¹⁴ and OR¹⁴:
- R¹⁴ is selected from hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; cycloalkyl; cycloalkynyl; aryl; heterocyclic; arylalkyl; heterocyclic-alkyl; acyloxyalkyl; wherein said alkyl, alkenyl and alkynyl optionally contain one or more heteroatoms in or at the end of the hydrocarbon chain, said heteroatoms being independently selected from the group consisting of oxygen, sulfur and nitrogen;
 - R¹⁶, R¹⁷ and R¹⁸ are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; cycloalkenyl; cycloalkynyl; aryl; arylalkyl; heterocyclic ring; heterocyclic ring-alkyl; acyloxyalkyl; wherein said alkyl, alkenyl and alkynyl optionally contain one or more heteroatoms in or at the end of the hydrocarbon chain, said heteroatoms being independently selected from the group consisting of oxygen, sulfur and nitrogen;
 - X⁴ and R¹, or X⁵ and R² may together form an amino-acid residue or polypeptide wherein a carboxyl function of said amino-acid residue being at a distance from the amidate nitrogen not further than 5 atoms is esterified;

- X^4 and R^1 or X^5 and R^2 may together form a group having the formula $OC(R^9)_2OC(O)Y(R^{10})_a$ wherein Y = N or O, a = 1 when Y is O and a = 1 or 2 when Y is N;
- R⁹ is selected from the group consisting of hydrogen, alkyl, aryl, alkenyl, alkynyl, alkenylaryl, alkynylaryl or alkylaryl, wherein each of said alkyl, alkenyl, alkynyl and aryl groups is optionally substituted with one or more atoms or groups selected from the group consisting of halo, cyano, azido, nitro and OR¹⁴:

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- R¹⁰ is selected from the group consisting of hydrogen, alkyl, aryl, alkenyl, alkynyl, alkenylaryl, alkynylaryl and alkylaryl, wherein each of said alkyl, alkenyl, alkynyl and aryl groups is optionally substituted with one or more atoms or groups selected from the group consisting of halo, cyano, azido, nitro, OR¹⁴ and NR¹¹R¹²;
- R¹¹ and R¹² are each independently selected from the group consisting of hydrogen and alkyl, provided that at least one of R¹¹ and R¹² is not hydrogen;
 - n is an integer representing the number of methylene groups between and P, each of said methylene groups being optionally and independently substituted with one or two substituents selected from the group consisting of halogen, hydroxyl, sulhydryl and C₁₋₄ alkyl, and n being selected from 1, 2, 3, 4, 5 and 6; and
 - m is 0 or 1, including pharmaceutically acceptable salts, solvates, isomers and prodrugs thereof.
- 25 2. A compound according to claim 1, being represented by one of the general formulae (III) to (XVIII):

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$$R^{2}X^{5} \xrightarrow{X^{3}} R^{7} \xrightarrow{R^{6}} R^{5}$$

$$X^{1} \xrightarrow{B} B$$

$$X^{2}X^{5} \xrightarrow{R^{4}} R^{4}$$

$$X^{4}R^{1} \qquad (III),$$

$$R^{2}X^{5} \xrightarrow{P} R^{1}$$

$$X^{3}$$

$$R^{7}$$

$$R^{7}$$

$$R^{3}$$

$$R^{6}$$

$$R^{5}$$

 $R^{2}X^{5}$ $R^{2}X^{5}$ R^{3} R^{7} R^{7} R^{8} R^{7} R^{7} R^{8} R^{7} R^{7} R^{8} R^{7} R^{7} R^{8} R^{7} R^{8} R^{7} R^{8} R^{7} R^{8} R^{7} R^{8} R^{7} R^{8} R^{8}

$$\mathbb{R}^{2} \mathbb{X}^{5}$$
 \mathbb{R}^{3}
 \mathbb{R}^{7}
 \mathbb{R}^{6}
 \mathbb{R}^{5}
 \mathbb{R}^{4}
 \mathbb{R}^{6}
 \mathbb{R}^{5}
 \mathbb{R}^{4}
 \mathbb{R}^{1}
 \mathbb{R}^{1}
 \mathbb{R}^{1}
 $\mathbb{R}^{2} \mathbb{R}^{1}$
 $\mathbb{R}^{2} \mathbb{R}^{1}$
 $\mathbb{R}^{2} \mathbb{R}^{1}$

$$R^{2}X^{5} \longrightarrow X^{4}R^{1}$$

$$R^{3} \longrightarrow X^{4}R^{1}$$

$$R^{4} \longrightarrow X^{4}R^{1}$$

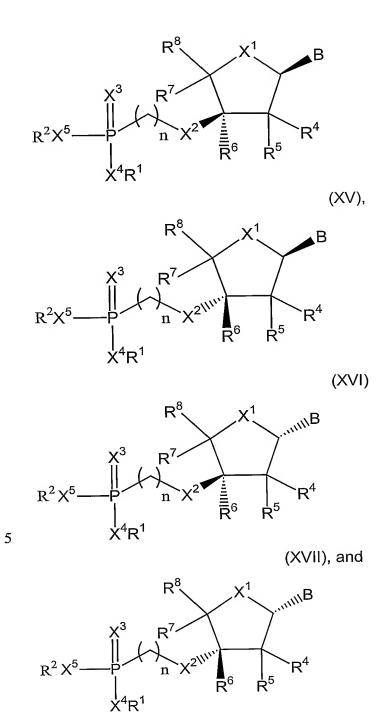
$$R^{5} \longrightarrow X^{5} \longrightarrow X^{5}$$

$$R^{5} \longrightarrow X^{5} \longrightarrow X^{5} \longrightarrow X^{5}$$

$$R^{5} \longrightarrow X^{5} \longrightarrow X^{5} \longrightarrow X^{5}$$

$$R^{5} \longrightarrow X^{5} \longrightarrow X^{5} \longrightarrow X^{5} \longrightarrow X^{5}$$

$$R^{5} \longrightarrow X^{5} \longrightarrow X^$$



wherein n, m, B, X¹, X², X³, X⁴, X⁵, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹⁴, R¹⁶, R¹⁷ and R¹⁸ are defined as in formula (II), including pharmaceutically acceptable salts, solvates, isomers and prodrugs thereof.

(XVIII)

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3. A compound according to claim 1, being represented by any of the following formulae (XX) to (XXVI):

$$R^{8}$$
 X^{1}
 R^{7}
 X^{3}
 R^{7}
 X^{4}
 X^{4}
 X^{4}
 X^{4}
 X^{4}
 X^{5}
 X^{7}
 X^{7}
 X^{7}
 X^{8}
 X^{7}
 X^{1}
 X^{1}
 X^{2}
 X^{3}
 X^{4}
 X^{7}
 X^{2}
 X^{4}
 X^{4

$$X^3$$
 X^4
 X^4

10 (XXII),

$$R^2X^5$$
 R^4
 X^4R^1

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$$R^{8}$$
 R^{7}
 R^{8}
 R^{7}
 R^{4}
 R^{4}
 R^{5}
 R^{7}
 R^{8}
 R^{7}

5 (XXV), and

$$R^{8}$$
 X^{1}
 B
 R^{2}
 X^{5}
 X^{4}
 X^{1}
 X^{2}
 X^{4}
 X^{1}
 X^{2}
 X^{4}
 X^{1}
 X^{2}
 X^{4}
 X^{1}
 X^{2}
 X^{3}
 X^{4}
 X^{1}
 X^{2}
 X^{4}
 X^{1}
 X^{2}
 X^{3}
 X^{4}
 X^{4}

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wherein n, m, B, X¹, X², X³, X⁴, X⁵, R¹, R², R³, R⁴, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹⁴, R¹⁶, R¹⁷ and R¹⁸ are defined as in formula (II), including pharmaceutically acceptable salts, solvates, isomers and prodrugs thereof.

4. A compound according to any of claims 1 to 3, wherein B is selected from the group consisting of hypoxanthine, guanine, adenine, cytosine, inosine, thymine, uracil, xanthine, 8-aza derivatives of 2-aminopurine, 2,6-

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diaminopurine, 2-amino-6-chloropurine, hypoxanthine, inosine and xanthine; derivatives of adenine, guanine, 2-aminopurine, 7-deaza-8-aza diaminopurine, 2-amino-6-chloropurine, hypoxanthine, inosine and xanthine; derivatives of 2-aminopurine, 2,6-diaminopurine, 2-amino-6chloropurine, hypoxanthine, inosine and xanthine; 7-deaza derivatives of 2-2-amino-6-chloropurine, hypoxanthine, 2,6-diaminopurine, aminopurine, 2-aminopurine, 2,6of derivatives 3-deaza xanthine; inosine and diaminopurine, 2-amino-6-chloropurine, hypoxanthine, inosine and xanthine; 5-5-iodocytosine; 5-fluorocytosine; 5-chlorocytosine; 6-azacytosine; 5-5-bromovinyluracil; 5-fluorouracil; 5-methylcytosine; bromocytosine; 5-trifluoromethyluracil; 5-5-bromouracil; 5-iodouracil; chlorouracil; methoxymethyluracil; 5-ethynyluracil and 5-propynyluracil.

A compound represented by one of the following general formulae (XXVII) to (XXXVI):

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(XXIX),

wherein:

- U is an acyl group,
- V is a silyl group,
- 10 W is an alkyl group,
 - the snake-like symbol means any stereochemical arrangement of the respective bond,
 - B^p is an optionally protected heterocyclic nucleobase, and
- Phos is an O-protected phosphonoalkoxy group or S-protected phosphonothioalkyl group.
 - 6. Use of a compound according to claim 5 as an intermediate for making a compound according to any of claims 1 to 4.

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- 7. A compound according to any of claims 1 to 4, being selected from the group consisting of: 1-(N⁶-benzoyladenin-9-yl)-2-O-benzoyl-3-O-(diisopropylphosphonomethyl)-Lthreose (11); 1-(thymin-1-yl)-2-O-benzoyl-3-O-(diisopropylphosphonomethyl)-L-threose(12); 5 1-(uracil-1-yl)-2-O-benzoyl-3-O-(diisopropylphosphonomethyl)-L-threose (13); 1-(N⁴-acetylcytosin-1-yl)-2-O-benzoyl-3-O-(diisopropylphosphonomethyl)-Lthreose (14); 1-(adenin-9-yl)-3-O-(diisopropylphosphonomethyl)-L-threose (15); 1-(thymin-1-yl)-3-O-(diisopropylphosphonomethyl)-L-threose (16); 10 1-(uracil-1-yl)-3-O-(diisopropylphosphonomethyl)-L-threose (17); 1-(cytosin-1-vI)-3-O-(diisopropylphosphonomethyl)-L-threose (18); 1-(adenin-9-yl)-2-deoxy-3-O-(diisopropylphosphonomethyl)-L-threose (19); 1-(thymin-1-yl)-2-deoxy-3-O-(diisopropylphosphonomethyl)-L-threose (20); 1-(uracil-1-yl)-2-deoxy-3-O-(diisopropylphosphonomethyl)-L-threose (21); 15 1-(cytosin-1-yl)-2-deoxy-3-O-(diisopropylphosphonomethyl)-L-threose (22); 1-(adenin-9-yl)-3-O-(phosphonomethyl)-L-threose sodium salt (3a); 1-(thymin-1-yl)-3-O-(phosphonomethyl)-L-threose sodium salt (3b); 1-(uracil-1-yl)-3-O-(phosphonomethyl)-L-threose sodium salt (3c); 1-(cytosin-1-yl)-3-O-(phosphonomethyl)-L-threose sodium salt (3d); 20 1-(adenin-1-yl)-2-deoxy-3-O-(phosphonomethyl)-L-threose sodium salt (3e); 1-(thymin-1-yl)-2-deoxy-3-O-(phosphonomethyl)-L-threose sodium salt (3f); 1-(uracil-1-vl)-2-deoxy-3-O-(phosphonomethyl)-L-threose sodium salt (3g);
 - 7. The use of a compound according to any of the claims 1 to 4, for the manufacture of a medicament for the prevention or treatment of a viral infection in a mammal.

1-(cytidin-1-yl)-2-deoxy-3-O-(phosphonomethyl)-L-threose sodium salt (**3h**); a pharmaceutically acceptable salt, an isomer, a solvate or a prodrug thereof.

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- 8. The use according to claim 7, wherein said viral infection is an infection by the Human Immunodeficiency Virus (HIV).
- 9. A pharmaceutical composition comprising a compound according to any of the claims 1 to 4 as an active ingredient in admixture with at least a pharmaceutically acceptable carrier.
 - 10.A pharmaceutical composition according to claim 9, further comprising an antiviral agent.

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11.A method of treatment or prevention of a viral infection in a mammal, comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound according to any of claims 1 to 4.